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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/729,667      | 12/05/2003  | Larry Gold           | NEX71/D             | 3271             |

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EXAMINER

WESSENDORF, TERESA D

ART UNIT PAPER NUMBER

1639

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                                      |                                    |  |
|------------------------------|--------------------------------------|------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/729,667 | <b>Applicant(s)</b><br>GOLD, LARRY |  |
|                              | <b>Examiner</b><br>T. D. Wessendorf  | <b>Art Unit</b><br>1639            |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16 is/are pending in the application.  
     4a) Of the above claim(s) 4,7,9,10,12,13 and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-8,11,14 and 15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____.  |

**DETAILED ACTION*****Election/Restrictions***

Applicant's election with traverse of the following species: at least one binding domain is an aptamer (see claim 2), the linker is polyethylene glycol (see claim 7), the aptamer binding domain is coupled at the 3' end to the other binding domain (see claim 8), the aptamer binding domain, unmodified, and the 7TM-GPCR is the neurotensin A receptor (see claim 11). in the reply filed on 10/26/04 is acknowledged. The traversal is on the ground(s) that all of the claims of the application are drawn to bivalent binding molecules comprising two or more binding domains to two or more epitopes of the same transmembrane G-protein-coupled receptor, wherein the binding domains are coupled to each other, as recited in claim 1. Thus, all of the claims define the same essential characteristics of a single disclosed embodiment of the invention. The individual claims of the application "are but different definitions of the same disclosed subject matter, varying in breadth or scope of definition." MPEP 806.03. Each of the dependent claims e.g., 2-7 narrow the scope of the subject matter of claim 1. This is not found persuasive because the election/restriction is based on species that are of different scope, more than simply on its definition. The species are

Art Unit: 1639

structurally distinct compounds. The examination of all the species would present an undue burden of examination. A prior art reference anticipating one species would not render obvious a structurally different species. However, upon reconsideration of applicant's arguments and restriction/election, the restriction/election with respect to the G-protein coupled receptors are withdrawn.

#### ***Status of Claims***

Claims 1-16 are pending.

Claims 4, 7 (with respect to the non-elected species), 9-10, 11, 12-13 and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/26/04.

Claims 1-3, 5-8, 11 and 14-15 are under examination.

#### ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors.

Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-8, 11 and 14-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to provide an adequate written description of a bivalent binding molecule. The specification does not describe any bivalent binding molecule either by structure or formula except by its claimed function. In patent applications, Examples normally provide the details of the actual work done by the inventor. It is this Example that provides guidance to one skilled in the art whether applicant is in possession of the claimed invention. However, the Examples do not describe any bivalent binding molecule. It describes methods

Art Unit: 1639

of obtaining the epitope receptors and libraries that bind to it. The libraries are supposed to produce the bivalent molecule. However, it is not apparent from this procedure the bivalent binding molecule obtained. Except for the definition in the specification as to a "bivalent binding molecule", no structure or formula for a single bivalent binding molecule is disclosed. The law clearly indicates that a patent specification must describe the claimed invention in **sufficient detail** (not in general terms). An applicant shows possession of the claimed invention by describing the claimed invention with all of its **limitations** using such descriptive means as words, structures and formulas to show that the invention is complete. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQM 1961, 1966 (Fed. Cir. 1997); MPEP 2163. The general statements in the specification are therefore not a detail description of the invention. A "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". *University of California v. Eli Lilly and Co.*, 43 USPQ 2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993) [The claims at issue in *University of California v. Eli Lilly*

Art Unit: 1639

defined the invention by function of the claimed DNA (encoding insulin)].

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 6 and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by Lerner et al (WO98/03632). [This rejection is based on the broad claimed bivalent binding molecule i.e., not as aptamer(s)].

Lerner discloses e.g., at page 10, lines 7-11 a bivalent molecule that binds to G-protein coupled receptors (GPCR) wherein said binding of the bivalent molecule (agonist or antagonist or combination thereof) to the same or different GPCRs surprisingly produces a synergistically higher binding than that of the two individual [agonist] ligands. The different bivalent molecules are disclosed at page 11, lines 11-18 (e.g., neurotensin). Lerner at page 17, line 23 up to page 18, line 30 discloses a spacer (i.e., linker, as claimed) e.g., polyethylene glycol. Furthermore, Lerner e.g., at page 13, lines

Art Unit: 1639

18-24 discloses that the two ligands have selective binding affinity for one type of GPCR or that the two ligands can be non-identical and are selective for different types of GPCRs. See the specific bivalent molecules in the Examples at pages 36-38 and the claims.

[Applicant is not entitled to the priority date of 4/28/1994 of application 08/234,997 ('997 application) since the '997 application does not disclose a bivalent binding molecule to 7T G-protein -coupled receptor.]

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5-8, 11 and 14-15 are rejected under 35 U.S.C. 103(a) as being obvious over Biesecker et al (5,683,867) in view of Lerner et al (WO98/03632) and Toole (WO 92/14843).



Art Unit: 1639

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(1)(1) and § 706.02(1)(2).

Art Unit: 1639

Biesecker discloses e.g., at col. 19, claims 6-7, 10-11 and 14 a blended nucleic acid ligand (i.e., a bivalent binding molecule, as claimed) comprising of RGD-RNA that binds to gpIIb/IIIa. See also e.g., col. 12, Example 2 up to col. 13, line 60. Biesecker does not teach a bivalent binding molecule that binds to the 7TM G-protein coupled receptor. However, Lerner discloses e.g., at page 13, lines 18-24 that the two ligands of a bivalent molecule that binds to the G-protein coupled receptors (as neurotensin) have selective binding affinity for one type of GPCR or that the two ligands can be non-identical and are selective for different types of GPCRs that surprisingly produces a synergistically higher binding than that of the two individual molecules. Toole discloses and provides a list of different aptamer binding receptors such as that aptamers binding to 7TM G-protein coupled receptors such as the extracellular proteins of 7TMG-protein like bradykinin, integrin receptors gpIIb/IIIa (page 141, Table 1) and etc. It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to identify bivalent molecule that binds to 7TM GPCR in the method of Biesecker as taught by Lerner. Lerner provides the motivation in that the bivalent binding molecule produces synergistic binding relative to the individual components of the bivalent molecule.

Art Unit: 1639

[See applicants' apparent recognition of this fact at paragraph bridging pages 3 and 4 of the instant disclosure. It states "...Bivalency can allow antibodies to bind to multimeric antigens with great avidity; multivalency theoretically can increase apparent binding affinity by several orders of magnitude (Crothers, D.M. et al., *Immunochemistry*, 341-351 (1972))...". The different GPCRs are also disclosed by Lerner which is similarly disclosed by Toole. The recited function of the known bivalent or blended aptamer-peptide in the prior art i.e., binding to 7TM-GPCR, does not cause a claim drawn to such function to distinguish over the prior art.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Art Unit: 1639

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 5-8, 11 and 14-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6, 7, 10-11, and 14 of U.S. Patent No. 5,683,867 (Biesecker et al) in view of Lerner and Toole.

See the rejection under the obviousness rejection above.

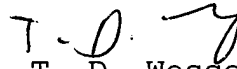
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Art Unit: 1639

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
T. D. Wessendorf  
Primary Examiner  
Art Unit 1639

Tdw  
January 24, 2005